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Synthesis and a Novel Fragmentation of 6-Alkoxy-5,6-dihydro-4*H*-1,2-oxazine 2-Oxide

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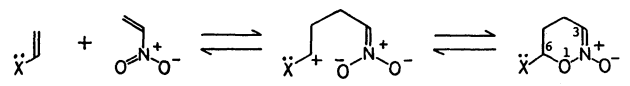
An electron-deficient nitro olefin, methyl α,p-dinitrocinnamate, reacts with vinyl ethers to give cyclic nitronic esters, which are stable as compared with those produced by reactions of nitro olefins with enamines. Stability of the cyclic nitronate depends on the properties of the substituents at 4- and 6-positions of the ring. The adducts undergo fragmentation by a catalytic amount of base to β,γ-unsaturated α-hydroxyimino esters.

A cyclic nitronic ester, 5,6-dihydro-4*H*-1,2-oxazine 2-oxide, has been known as an interesting intermediate which can be converted into nitroalkylated enamines,[1] 1,4-diones,[2] and so forth[3] via easy heterolytic cleavage of the O(1)-C(6) bond. Such cyclic compounds are easily obtainable by reactions of simple nitro olefins with enamines,[1] silyl enol ethers,[2] enolate anions,[4] or cyclohexene,[5] although little has been clarified on the chemical properties of them except for the O(1)-C(6) bond cleavage owing to their thermal and hydrolytic instability. In order to investigate further reactivities of the dihydrooxazine *N*-oxide, we wished to prepare stable cyclo adducts by reaction of nitro olefins with vinyl ethers. The dihydrooxazine *N*-oxide might be stable if the carbocation formed by the bond cleavage of the compound would be unstable (Scheme 1) or, in other words, if the substituent X in Scheme 1 would be less electron-donating. Direct reaction of simple nitro olefins with vinyl ethers failed, however, to give adducts because of low nucleophilicity of the latters. Another strategy to prepare the stable cycloadduct may be usage of highly electrophilic nitro olefins. We report here cycloaddition of an electron-deficient nitro olefin, methyl α,p-dinitrocinnamate (**1**), with vinyl ethers, and some properties of the cycloadducts.

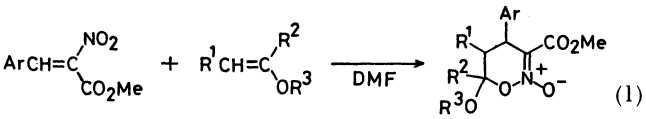


Scheme 1.

Results and Discussion

Reaction of **1** with ethyl vinyl ether in DMF at room temperature gave a diastereomeric mixture **2** of two cycloadducts in 92% yield. The ^{1}H NMR spectra of the isomers **2a** and **2b** reveal that they have cyclic structures rather than the alternative linear ones, methyl 5-ethoxy-2-nitro-3-(*p*-nitrophenyl)-2-, 3-, or 4-pentenoates. The ratio of the isomers **2a** and **2b** was about 4 : 1 regardless of the configurations of the nitro olefin. The results are consistent with the mechanism of the step wise cyclization shown in Scheme 1. The small coupling constants (ca. 3.5 Hz) between 6-H and 5- or 5′-H of both isomers show that the 6-ethoxyl group is in an axial position of a pseudo chair ring. The configuration may be rationalized by the strong anomeric effect of the ring.[6] A difference between the spectra of **2a** and **2b** lies in the coupling patterns of 4-H ($J_{4,5}$ and $J_{4,5'}$=3.5 Hz and 8.7 Hz for **2a**; $J_{4,5}$ and $J_{4,5'}$=8.7 Hz and 9.1 Hz for **2b**). This difference may arise from different configurations of the aryl group at C(4) of the ring. The aryl group of **2a** is in a pseudoaxial position, while that of **2b** is in a pseudoequatorial one. Another difference is observed in the ester stretching band (1705 cm^{-1} for **2a**; 1745 cm^{-1} for **2b**). The higher frequency of the carbonyl band of **2b** may be interpreted in terms of restricted conjugation between the ester and the nitronic ester groups due to steric repulsion between the ester and the aryl groups (Fig. 1). From these results the structures of **2a** and **2b** were assigned to *cis*- and *trans*-6-ethoxy-3-methoxycarbonyl-4-(*p*-nitrophenyl)-5,6-dihydro-4*H*-1,2-oxazine 2-oxide, respectively (Fig. 1).

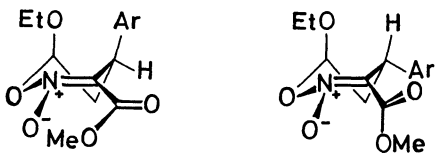
Other substituted vinyl ethers also reacted with **1** at higher temperatures to give the similar cyclic adducts **3**—**6** (Eq. 1 and Table 1). These substituted vinyl ethers did not reacted at room temperature because of the bulkiness of the reagents. The ^{1}H NMR and IR spectra of the adducts show that they are also a mixture of diastereomers, although details of their stereochemistry are not clear yet.



(1)

1 **2~6**

(Ar=*p*-$C_6H_4NO_2$)



2a **2b**

Fig. 1. Structures of the adducts **2a** and **2b**. (Ar=$C_6H_4NO_2$-*p*)

Table 1. Cycloaddition of Methyl α,*p*-Dinitrocinnamate (**1**) with Vinyl Ethers

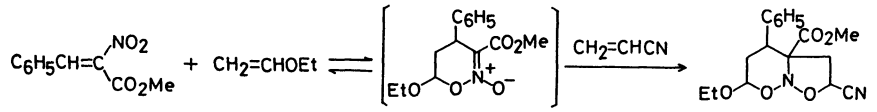
Vinyl ether	Reaction conditions		Product	Decomp temp/°C	Yield/%
	Temp./°C	Time/h			
Ethyl vinyl ether	r.t.	24	**2**	124—127	92
2,3-Dihydrofuran	60	12	**3**	148—153	80
3,4-Dihydro-2*H*-pyran	60	12	**4**	140—143	30
1-Methoxycyclopentene	50	12	**5**	141—144	84
1-Methoxycyclohexene	50	12	**6**	174—175	72

When **1** was reacted with 1-morpholinocyclohexene at 0 °C in benzene, an unstable adduct, which was assumed to be a dihydrooxazine *N*-oxide derivative, was precipitated. It spontaneously decomposed into the Michael adduct in benzene solution as well as other cyclic adducts of nitro olefins with enamines.[1] On the contrary, the adducts **2—6** were very stable even at 100 °C. This fact indicates that the stability of the dihydrooxazine *N*-oxide structure depends on the electronic properties of the substituents at C(6) as expected.

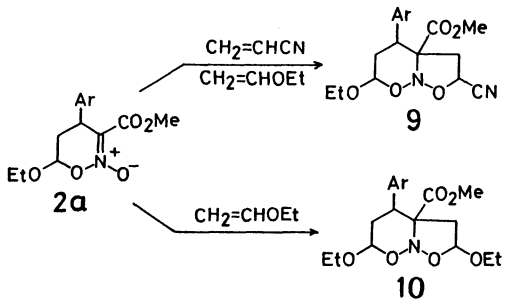
Reactions of methyl α-nitrocinnamate (**7**) or less electrophilic nitro olefins such as methyl β-methoxy-α-nitroacrylate or β,*p*-dinitrostyrene, with ethyl vinyl ether did not give the corresponding 1 : 1 cycloadducts even at higher temperatures. On the other hand, treatment of **7** with ethyl vinyl ether in the presence of acrylonitrile at 70 °C in DMF gave an 1 : 1 : 1 adduct **8** in 57% yield (Eq. 2). The role of the acrylonitrile is to trap an unstable dihydrooxazine *N*-oxide by 1,3-dipolar addition, because **2a** also reacted with acrylonitrile even in the presence of ethyl vinyl ether to give the corresponding 1 : 1 : 1 adduct **9** (Eq. 3). In the absence of acrylonitrile, the reaction of **2a** with ethyl vinyl ether gave an 1 : 2 adduct **10** at 70 °C in DMF. These reactions are consistent with the reactivity of nitronic esters as an electron-rich 1,3-dipole.[7] The 1 : 1 cycloadduct of **7** with ethyl vinyl ether (see Eq. 2) could not be isolated in contrast with the stable nitronate **2**. The fact implies that the stability of the dihydrooxazine *N*-oxide seems to be affected by the C(4)-substituent as well as the C(6)-one.

Methanolysis of **2a** and **2b** under acidic conditions gave the same product, methyl 5,5-dimethoxy-2-nitro-3-(*p*-nitrophenyl)pentanoate as a result of the common O(1)-C(6) bond cleavage.[1-4]

Treatment of **2a** by a catalytic amount of sodium hydroxide in DMSO-d_6 at room temperature gave ethyl formate and methyl 2-hydroxyimino-3-(*p*-nitrophenyl)-3-butenoate (**11**), immediately and quantitatively. Ammonia was a less efficient catalyst because of poor yield of **11**. Bulky triethylamine did not give any products even at a reflux temperature of THF. On the other hand, the stereoisomer **2b** gave neither **11** nor **8** under the corresponding reaction conditions. These results may be attributed to the steric hinderance around the nitronic ester moiety of **2b** as mentioned above. Although the adducts **2—6** are mixtures of diastereomers, they also gave the fragmentation products **11—15** in good to moderate yields by treatment with sodium methoxide (Eq. 4 and Table 2). The formation of the products **12** and **13** may proceed via easy hydrolysis of the initially formed formate given in Eq. 4. On the basis of these results, the rate-determinig step of the fragmentation may be deprotonation of 4-H of the ring. Such a reaction of the 5,6-dihydro-4*H*-1,2-oxazine 2-oxides has not been known yet, while the similar fragmentation of some related compounds, 5-thia analogues[8] or N-alkyl salts[9] of 5,6-dihydro-4*H*-1,2-oxazine have been reported. Most of the reported reactions of the dihydrooxazine *N*-oxides with strong bases also proceed via the O(1)-C(6) bond cleavage.[1a,4] Stability of the O(1)-C(6) bond may be one of the important factors of this fragmentation.

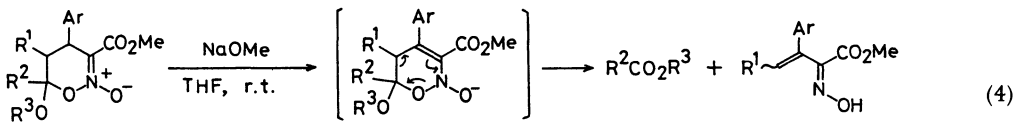


7 8 (2)



2a 9 10 (3)

(Ar=$C_6H_4NO_2$-*p*)



2~6 11~15 (4)

(Ar=$C_6H_4NO_2$-*p*)

Table 2. Fragmentation of 6-Alkoxy-5,6-dihydro-4*H*-1,2-oxazine 2-Oxides by Sodium Methoxide

Substrate	Product	R^1	Mp θ_m/°C	Yield/%
2	**11**	H	149.5—151.5	82
3	**12**	$(CH_2)_2OH$[a)]	140.5—144.5	25
4	**13**	$(CH_2)_3OH$[a)]	96.5—98.5	80
5	**14**	$(CH_2)_3CO_2Me$	98.5—99.0	78
6	**15**	$(CH_2)_4CO_2Me$	Oil	64

a) The isolated products were given by hydrolysis of the initial products [R^1=$[(CH_2)_nOCOH]$ under the reaction conditions.

Reduction of **2a** and **2b** by triethyl phosphite gave the corresponding isomers of 2-deoxygenated products, **16a** and **16b**, respectively. Treatment of **16a** with a catalytic amount of sodium methoxide in THF gave the other isomer **16b** in 42% yield probably via deprotonation of 4-H of the ring. However the similar fragmentation of **16b** shown by Eq. 4 did not occur at all. Reported transformations of other 5,6-dihydro-4*H*-1,2-oxazines[10] are also quite different from this fragmentation. Consequently the *N*-oxide function of the adducts must play a significant role in the fragmentation.

The present fragmentation is a unique reaction of stable 5,6-dihydro-4*H*-1,2-oxazine 2-oxides.

Experimental

The infrared spectra were measured in nujol by means of a Hitachi 260-10 spectrophotometer and the ^{1}H NMR spectra were taken on a Hitachi R-20B spectrometer.

Methyl α,*p*-Dinitrocinnamate (1). This nitro olefin was prepared by the method of Dornow[11] in 72% yield (E : Z=3 : 4 by ^{1}H NMR). Fractional recrystallization from CCl_4 gave each isomer. E Isomer: Pale yellow needles; mp 135—138 °C. ^{1}H NMR ($CDCl_3$) δ=3.96 (s, 3H), 7.69 (d, 2H, *J*=8.9 Hz), 8.12 (s, 1H), 8.31 (d, 2H, *J*=8.9 Hz). IR: 1740 cm^{-1} (C=O), 1520, 1350 cm^{-1} (NO_2). Found: C, 47.57; H, 3.21; N, 10.98%. Calcd for $C_{10}H_8H_2O_6$: C, 47.62; H, 3.20; N, 11.11%. Z Isomer: Pale yellow needles; mp 125—130 °C. ^{1}H NMR ($CDCl_3$) δ=3.97 (s, 3H), 7.60 (d, 2H, *J*=8.6 Hz), 7.63 (s, 1H), 8.28 (d, 2H, *J*=8.6 Hz). IR: 1720 cm^{-1} (C=O), 1550, 1535, 1340 cm^{-1} (NO_2). Found: C, 47.50; H, 3.14; N, 11.13%. Calcd for $C_{10}H_8N_2O_6$: C, 47.62; H, 3.20; N, 11.11%.

Reaction of 1 with Ethyl Vinyl Ether. A solution of 2.52 g (10 mmol) of **1** and 3.60 g (50 mmol) of ethyl vinyl ether in 20 ml of DMF was allowed to stand for 1 d. After the solvent was removed in vacuo the residual solid was recrystallized from benzene-hexane to give 2.98 g (92%) of a diastereomeric mixture (**2a** : **2b**=4 : 1) of 6-ethoxy-3-methoxycarbonyl-4-(*p*-nitrophenyl)-5,6-dihydro-4*H*-1,2-oxazine 2-oxide (**2**). Fractional recrystallization of **2** from benzene-hexane gave each isomer.

2a (cis isomer): Colorless prisms; mp 124—126 °C (decomp). ^{1}H NMR ($CDCl_3$) δ=1.18 (t, 3H, *J*=7.1 Hz), 2.26 (td, 1H, *J*=3.5 Hz and 14.3 Hz), 2.65 (ddd, 1H, *J*=3.5 Hz, 8.7 Hz, and 14.3 Hz), 3.70 (s, 3H), 3.8 (m, 2H), 4.50 (dd, 1H, *J*=3.5 Hz and 8.7 Hz), 5.48 (t, 1H, *J*=3.5 Hz), 7.46 (d, 2H, *J*=8.8 Hz), 8.16 (d, 2H, *J*=8.8 Hz). IR: 1705 cm^{-1} (C=O), 1595 cm^{-1} (C=N), 1520, 1345 cm^{-1} (NO_2). Found: C, 51.78; H, 4.93; N, 8.57%. Calcd for $C_{14}H_{16}N_2O_7$: C, 51.85; H, 4.97; N, 8.64%.

2b (trans isomer): Colorless prisms; mp 137—139 °C (decomp). ^{1}H NMR ($CDCl_3$) δ=1.29 (t, 3H, *J*=7.0 Hz), 2.34 (dd, 1H, *J*=9.1 Hz and 3.9 Hz), 2.40 (dd, 1H, *J*=8.7 Hz and 3.0 Hz), 3.70 (s, 3H), 3.77 (qd, 1H, *J*=7.0 Hz and 9.7 Hz), 4.07 (qd, 1H, *J*=7.0 Hz and 9.7 Hz), 4.54 (dd, 1H, *J*=8.7 Hz and 9.1 Hz), 5.50 (dd, 1H, *J*=3.0 Hz and 3.7 Hz), 7.44 (d, 2H, *J*=8.4 Hz), 8.20 (d, 2H, *J*=8.4 Hz). IR: 1745 cm^{-1} (C=O), 1590 cm^{-1} (C=N), 1520, 1350 cm^{-1} (NO_2). Found: C, 51.72; H, 4.95; N, 8.64%. Calcd for $C_{14}H_{16}N_2O_7$: C, 51.85; H, 4.97; N, 8.64%.

Reaction of 1 with 2,3-Dihydrofuran. A solution of 2,3-dihydrofuran (2.90 g, 41.4 mmol) and **1** (1.34 g, 5.3 mmol) in 6 ml of DMF was heated at 60 °C for 12 h. After removal of the solvent, residual solid was recrystallized from benzene-hexane to give 1.37 g (80%) of a diastereomeric mixture of **3** [mp 148—153 °C (decomp), IR: 1730 and 1700 cm^{-1}]. Recrystallization of **3** from ether gave one of the isomers **3b**; colorless prisms; mp 150—154 °C (decomp). ^{1}H NMR ($CDCl_3$) δ=1.8—2.7 (m, 2H), 3.1—3.6 (m, 1H), 3.91 (s, 3H), 3.9—4.3 (m, 2H), 4.63 (m, 1H), 5.94 (d, 1H, *J*=7.0 Hz), 7.50 (d, 2H, *J*=8.5 Hz), 8.20 (d, 2H, *J*=8.5 Hz). IR: 1730 cm^{-1} (C=O), 1580 cm^{-1} (C=N), 1520, 1355 cm^{-1} (NO_2). Found: C, 52.50; H, 4.40; N, 8.40%. Calcd for $C_{14}H_{14}N_2O_7$: C, 52.17; H, 4.38; N, 8.69%.

Reactionof 1 with 3,4-Dihydro-2*H*-pyran. A solution of 2.77 g (11 mmol) of **1** and 4.62 g (55 mmol) of dihydropyran in 5 ml of DMF was heated at 60 °C for 12 h. After removal of the solvent in vacuo, residual oil was column-chromatographed on solica gel. The first eluent (chloroform-benzene 1 : 1) gave 0.83 g (30%) of the recovered nitro olefin. The second eluent (chloroform-acetone 20 : 1) gave 1.11 g (30%) of a diastereomeric mixture of the adduct **4** [mp 140—143 °C (decomp), IR: 1730, 1710, 1695 cm^{-1}]. Recrystallization of **4** from benzene-hexane gave an isomer **4a**; colorless powder; mp 142—145 °C (decomp). ^{1}H NMR ($CDCl_3$) δ=1.4—1.8 (m, 4H), 2.2—2.7 (m, 1H), 3.63 (s, 3H), 3.7—4.1 (m, 2H), 4.74 (d, 1H, *J*=8.4 Hz), 5.85 (m, 1H), 7.31 (d, 2H, *J*=8.7 Hz), 8.19 (d, 2H, *J*=8.7 Hz). IR: 1690 cm^{-1} (C=O), 1580 cm^{-1} (C=N), 1515, 1360, 1345 cm^{-1} (NO_2). Found: C, 53.33; H, 4.82; N, 8.43%. Calcd for $C_{15}H_{16}N_2O_7$: C, 53.57; H, 4.80; N, 8.33%.

Reaction of 1 with 1-Methoxyclopentene. A solution of 2.52 g (10 mmol) of **1** and 5.90 g (50 mmol) of 1-methoxycyclopentene in 10 ml of DMF was heated at 50 °C

for 12 h. After removal of the solvent in vacuo, the residue was recrystallized from benzene-hexane to give 2.93 g (83%) of the adduct **5**. Colorless needles; mp 141—144 °C (decomp). ^{1}H NMR ($CDCl_3$) δ=1.4—2.6 (m, 7H), 3.49 (s, 3H), 3.63 (s, 3H), 4.06 (d, 1H, J=4.5 Hz), 7.43 (d, 2H, J=8.8 Hz), 8.16 (d, 2H, J=8.8 Hz). IR: 1740, 1725 cm^{-1} (C=O), 1595 cm^{-1} (C=N), 1515, 1350 cm^{-1} (NO_2). Found: C, 54.91; H, 5.14; N, 7.95%. Calcd for $C_{16}H_{18}N_2O_7$: C, 54.85; H, 5.17; N, 7.99%. Similarly the adduct **6** was obtained from a reaction of **1** with 1-methoxycyclohexene. Colorless prisms; mp 174—175 °C (decomp). ^{1}H NMR ($CDCl_3$) δ=1.2—2.5 (m, 9H), 3.33 (s, 3H), 3.71 (s, 3H), 4.10 (s, 1H), 7.38 (d, 2H, J=9.0 Hz), 8.15 (d, 2H, J=9.0 Hz). IR: 1735 cm^{-1} (C=O), 1585 cm^{-1} (C=N), 1520, 1345 cm^{-1} (NO_2). Found: C, 56.15; H, 5.49; N, 7.55%. Calcd for $C_{17}H_{20}N_2O_7$: C, 56.04; H, 5.53; N, 7.69%.

Reaction of Methyl α-Nitrocinnamate (7) with Ethyl Vinyl Ether and Acrylonitrile. A solution of 0.41 g (2 mmol) of **7**, 0.32 g (6 mmol) of acrylonitrile, and 0.72 g (10 mmol) of ethyl vinyl ether in 5 ml of DMF was heated at 70 °C for 3 h. After removal of the solvent, residual oil was crystallized from benzene-hexane to give 0.38 g (57%) of 8-cyano-3-ethoxy-6-methoxycarbonyl-5-phenyl-2,9-dioxa-1-azabicyclo[4.3.0]nonane (**8**). Colorless needles; mp 165—174 °C. ^{1}H NMR ($CDCl_3$) δ=1.31 (t, 3H, J=7.0 Hz), 2.2 (ddd, 1H, J=13.0 Hz, 6.6 Hz, and 2.9 Hz), 2.5—4.2 (m, 6H), 3.42 (s, 3H), 5.02 (dd, 1H, J=7.7 Hz and 6.6 Hz), 5.31 (dd, 1H, J=10.2 Hz and 4.3 Hz), 7.0—7.4 (m, 5H). IR: 1740 cm^{-1} (C=O). Found: C, 61.13; H, 6.15; N, 8.40%. Calcd for $C_{17}H_{20}N_2O_5$: C, 61.43; H, 6.07: N, 8.43%.

Similarly, by a reaction of **2a** with acrylonitrile in the presence of ethyl vinyl ether, 8-cyano-3-ethoxy-6-methoxycarbonyl-5-(*p*-nitrophenyl)-2,9-dioxa-1-azabicyclo-[4.3.0]nonane (**9**) was obtained in 87% yield. Colorless powder; mp 210—218 °C. ^{1}H NMR (DMSO-d_6) δ=1.22 (t, 3H, J=7.2 Hz), 2.0—4.0 (m, 7H), 3.36 (s, 3H), 5.07 (t, 1H, J=7.3 Hz), 5.65 (dd, 1H, J=9.8 Hz and 4.7 Hz), 7.51 (d, 2H, J=8.9 Hz), 8.19 (d, 2H, J=8.9 Hz). IR: 1735 cm^{-1} (C=O), 1520, 1510, 1350, 1345 cm^{-1} (NO_2). Found: C, 54.30; H, 5.12; N, 11.03%. Calcd for $C_{17}H_{19}N_3O_7$: C, 54.11; H, 5.08; N, 11.14%.

Reaction of 2a with Ethyl Vinyl Ether. A solution of 0.65 g (2 mmol) of **2a** and 0.72 g (10 mmol) of ethyl vinyl ether in 5 ml of DMF was heated at 60 °C for 5 h. After removal of the solvent, residue was recrystallized from benzene-hexane to give 0.66 g (83%) of 3,8-diethoxy-6-methoxycarbonyl-5-(*p*-nitrophenyl)-2,9-dioxa-1-azabicyclo[4.3.0]nonane (**10**). Colorless needles; mp 174—175 °C. ^{1}H NMR ($CDCl_3$) δ=1.11 (t, 3H, J=7.0 Hz), 1.32 (t, 3H, J=7.0 Hz), 2.0—2.4 (m, 9H), 3.37 (s, 3H), 4.98 (t, 1H, J=7.0 Hz), 5.80 (d, 1H, J=6.0 Hz), 7.36 (d, 2H, J=8.6 Hz), 8.18 (d, 2H, J=8.6 Hz). IR: 1740 cm^{-1} (C=O), 1515, 1350 cm^{-1} (NO_2). Found: C, 54.33; H, 6.09; N, 7.01%. Calcd for $C_{18}H_{24}N_2O_8$: C, 54.55; H, 6.10; N, 7.10%.

Reaction of 1 with 1-Morpholinocyclohexene. To a solution of 1.66 g (6.6 mmol) of **1** in 60 ml of benzene, 1.10 g (6.6 mmol) of 1-morpholinocyclohexene in 10 ml of benzene was added at 0 °C. After 2 h, 0.55 g (20%) of colorless precipitate was obtained which was assumed to be a cyclo adduct. Decomp 80—81.5 °C. IR: 1730 cm^{-1} (C=O), 1565, 1520, 1345 cm^{-1} (NO_2). Residual benzene layer was crystallized from benzene-hexane to give 1.65 g (60%) of a mixture (1 : 1) of two diastereomers of methyl 3-(2-morpholino-2-cyclohexenyl)-2-nitro-3-(*p*-nitrophenyl)propanoate. Yellow powder; mp 120—124.5 °C. ^{1}H NMR ($CDCl_3$) δ=1.1—3.2 (m, 11H), 3.55 (s, 3H, ester methyl protons of one isomer), 3.80 (s, 3H, ester methyl protons of another isomer), 3.6—3.9 (m, 4H), 4.3 (m, 1H), 4.98 (t, 1H, J=3.9 Hz, an olefin proton of enamine), 5.86 (d, 1H, J=8.8 Hz, 2-H of one isomer), 6.02 (d, 1H, J=9.7 Hz, 2-H of another isomer), 7.44 (d, 2H, J=8.9 Hz, one isomer), 7.46 (d, 2H, J=8.9 Hz, another isomer), 8.11 (d, 2H, J=8.9 Hz). IR: 1745 cm^{-1} (C=O), 1650 cm^{-1} (C=C-N). Found: C, 57.28; H, 5.99: N, 9.87%. Calcd for $C_{20}H_{25}N_3O_7$: C, 57.27; H, 6.01; N, 10.02%.

Methanolysis of 2 by Acid Catalyst. A solution of 0.975 g (3 mmol) of **2a** and 0.057 g (0.3 mmol) of *p*-toluenesulfonic acid in 30 ml of dry methanol was refluxed for 4 h. After removal of the solvent, residual oil was dissolved in chloroform, washed with water, and dried over sodium sulfate. The crude product was recrystallized by benzene-hexane to give 0.72 g (70%) of one of the diastereomers of methyl 5,5-dimethoxy-2-nitro-3-(*p*-nitrophenyl)pentanoate. Colorless plates; mp 94—98 °C. ^{1}H NMR ($CDCl_3$) δ=1.9—2.3 (m, 2H), 3.22 (s, 3H), 3.26 (s, 3H), 3.89 (s, 3H), 3.7—4.2 (m, 2H), 5.47 (d, 1H, J=10.0 Hz), 7.51 (d, 2H, J=8.7 Hz), 8.24 (d, 2H, J=8.7 Hz). IR: 1760 cm^{-1} (C=O), 1565, 1520, 1350 cm^{-1} (NO_2). Found: C, 49.35; H, 5.29; N, 8.16%. Calcd for $C_{14}H_{18}N_2O_8$: C, 49.12; H, 5.30; N, 8.18%. The similar treatment of **2b** gave the same product in 67% yield.

Fragmentation of the Adduct 2 by Sodium Methoxide. To a solution of 0.65 g (2 mmol) of **2** in 30 ml of THF at −15 °C, 1 ml (0.35 mmol) of sodium methoxide in methanol solution was added. The solution turned to red and was allowed to stand at room temperature for 30 min. An equimolar amount of hydrogen chloride (methanol solution, 0.8 mol dm^{-3}) was added to the solution and the solvent was removed under reduced pressure. The residue was dissolved in chloroform, washed with water, and dried over magnesium sulfate. After removal of the solvent, residual solid was recrystallized from benzene-hexane to give 0.41 g (82%) of methyl 2-hydroxyimino-3-(*p*-nitrophenyl)-3-butenoate (**11**). Colorless prisms; mp 149.5—151.5 °C. ^{1}H NMR ($CDCl_3$) δ=3.85 (s, 3H), 5.59 (s, 1H), 5.68 (s, 1H), 7.46 (d, 2H, J=8.7 Hz), 8.13 (d, 2H, J=8.7 Hz), 8.54 (s, 1H). IR: 3320 cm^{-1} (O-H), 3120, 3090 cm^{-1} (vinyl C-H), 1730 cm^{-1} (C=O), 1510, 1345 cm^{-1} (NO_2). Found: C, 53.03; H, 4.07; N, 11.07%. Calcd for $C_{11}H_{10}N_2O_5$: C, 52.80; H, 4.03; N, 11.20%.

The similar treatment of the adducts **3—6** gave the oximes **12—15**, which were purified by column chromatography on silica gel. Acetone-chloroform elutes were recrystallized from benzene-hexane.

Methyl 6-Hydroxy-2-hydroxyimino-3-(*p*-nitrophenyl)-3-hexenoate (12): Colorless needles; mp 140.5—144.5 °C. ^{1}H NMR ($CDCl_3$) δ=2.4—2.8 (m, 3H), 3.69 (s, 3H), 3.7—4.0 (m, 2H), 6.41 (t, 1H, J=7.3 Hz), 7.51 (d, 2H, J=9.0 Hz), 8.21 (d, 2H, J=9.0 Hz), 11.6 (broad s, 1H). IR: 3250 cm^{-1} (O-H), 1740 cm^{-1} (C=O), 1510, 1350 cm^{-1} (NO_2). Found: C, 53.40; H, 4.87; N, 9.55%. Calcd for $C_{13}H_{14}N_2O_6$: C, 53.06; H, 4.80; N, 9.52%.

Methyl 7-Hydroxy-2-hydroxyimino-3-(*p*-nitrophenyl)-3-heptenoate (13): Colorless prisms; mp 96.5—98.5 °C. ^{1}H NMR ($CDCl_3$) A mixture of two configurational isomers A and B (A : B=3 : 2). A: δ=1.4—3.0 (m, 5H), 3.4—3.8 (m, 2H), 3.91 (s, 3H), 6.01 (t, 1H, J=7.7 Hz), 7.25 (d, 2H, J=8.7 Hz), 8.21 (d, 2H, J=8.7 Hz), 8.61 (s, 1H). B: δ=1.4—3.0 (m, 5H), 3.4—3.8 (m, 2H), 3.70 (s, 3H), 6.28 (t, 1H, J=8.0 Hz), 7.49 (d, 2H, J=8.7 Hz), 8.19 (d, 2H, J=8.7 Hz), 11.49 (s, 1H). IR: 3480, 3170 cm^{-1} (O-H), 1740, 1730 cm^{-1} (C=O), 1515,

1350 cm^{-1} (NO_2). Found: C, 54.79; H, 5.26; N, 9.12%. Calcd for $C_{14}H_{16}N_2O_6$: C, 54.54; H, 5.23; N, 9.09%.

Dimethyl 2-Hydroxyimino-3-(*p*-nitrophenyl)-3-octenedioate (14): Colorless prisms; mp 98.5—99 °C. ^1H NMR ($CDCl_3$) δ=1.5—2.5 (m, 6H), 3.59 (s, 3H), 3.88 (s, 3H), 5.95 (t, 1H, J=8.2 Hz), 7.31 (d, 2H, J=8.6 Hz), 8.20 (s, 1H), 8.22 (d, 2H, J=8.6 Hz). IR: 3300 cm^{-1} (O-H), 1735 cm^{-1} (C=O), 1520, 1350 cm^{-1} (NO_2). Found: C, 54.97; H, 5.23; N, 8.01%. Calcd for $C_{16}H_{18}N_2O_7$: C, 54.85; H, 5.17; N, 7.99%.

Dimethyl 2-Hydroxyimino-3-(*p*-nitrophenyl)-3-nonenedioate (15): Colorless oil. ^1H NMR ($CDCl_3$) δ=1.4—1.8 (m, 4H), 2.2—2.5 (m, 4H), 3.68 (s, 3H), 3.76 (s, 3H), 6.33 (t, 1H, J=7.5 Hz), 7.49 (d, 2H, J=9.1 Hz), 8.16 (d, 2H, J=9.1 Hz), 10.76 (s, 1H). IR: 3350 cm^{-1} (O-H), 1735 cm^{-1} (C=O), 1520, 1345 cm^{-1} (NO_2). Mass spectra: m/z 364 (M^+).

Reduction of 2 with Triethyl Phosphite. A solution of 0.65 g (2 mmol) of **2a** and 0.46 g (3 mmol) of triethyl phosphite in 10 ml of xylene was heated at 95 °C for 7.5 h under a nitrogen atmosphere. After removal of the solvent in vacuo, residue was recrystallized from benzene-hexane to give 0.47 g (76%) of *cis*-6-ethoxy-3-methoxycarbonyl-4-(*p*-nitrophenyl)-5,6-dihydro-4*H*-1,2-oxazine (**16a**): Colorless prisms; mp 91—92.5 °C. ^1H NMR ($CDCl_3$) δ=1.07 (t, 3H, J=7.0 Hz), 2.2—2.5 (m, 2H), 3.3—4.0 (m, 2H), 3.80 (s, 3H), 4.08 (dd, 1H, J=6.7 Hz and 4.0 Hz), 5.23 (t, 1H, J=3.2 Hz), 7.36 (d, 2H, J=9.1 Hz), 8.14 (d, 2H, J=9.1 Hz). IR: 1730 cm^{-1} (C=O), 1520, 1345 cm^{-1} (NO_2). Found: C, 54.44; H, 5.22; N, 8.97%. Calcd for $C_{14}H_{16}N_2O_6$: C, 54.54; H, 5.23; N, 9.09%.

Similarly, **16b** (trans isomer) was obtained by a reaction of **2b** with triethyl phosphite in 61% yield. Colorless powder; mp 101—103 °C. ^1H NMR ($CDCl_3$) δ=1.25 (t, 3H, J=6.9 Hz), 2.04 (ddd, 1H, J=13.6 Hz, 11.4 Hz, and 2.6 Hz), 2.38 (ddd, 1H, J=13.6 Hz, 7.8 Hz, and 2.6 Hz), 3.3—4.2 (m, 2H), 3.70 (s, 3H), 4.13 (dd, 1H, J=11.4 Hz and 7.8 Hz), 5.24 (t, 1H, J=2.6 Hz), 7.36 (d, 2H, J=9.0 Hz), 8.20 (d, 2H, J=9.0 Hz). IR: 1745 cm^{-1} (C=O), 1515, 1350 cm^{-1} (NO_2). Found: C, 54.33; H, 5.33; N, 8.89%. Calcd for $C_{14}H_{16}N_2O_6$: C, 54.54; H, 5.23; N, 9.09%.

Isomerization of 16a to 16b. Treatment of **16a** with sodium methoxide under the similar conditions of the fragmentation of **2a** with sodium methoxide gave **16b** in 42% yield.

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